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Preface

Modelling and analysis of biological systems —Based on papers presented at the Workshop on Membrane Computing and Biologically Inspired Process Calculi (MeCBIC) held in 2008 (Iasi), 2009 (Bologna) and 2010 (Jena)

The main aim of the MeCBIC (Membrane Computing and Biologically Inspired Process Calculi) series of workshops is to bring together researchers working on membrane computing and other biologically inspired formalisms, mainly process calculi and Petri nets, in order to communicate recent results and discuss new ideas concerning these formalisms as well as their properties and mutual relationships.

Biological membranes play a fundamental role in the complex reactions which take place in cells of living organisms. Membrane systems were introduced as a class of distributed parallel computing devices inspired by the observation that any biological system has a complex hierarchical structure, with a flow of biochemical substances and information that underlies their functioning. The modelling and analysis of biological systems has also attracted considerable interest from both process calculi and Petri net research communities. A deeper investigation of the relationships between these formalisms is both interesting and stimulating, and has already provided valuable cross fertilization of these research areas. Membrane computing deals with the computational properties, making use of automata, formal languages, and complexity results. Certain process calculi, such as mobile ambients and brane calculi, work also with notions of compartments and membranes. The emphasis is mainly on the faithful reflection of biological reality, and the central interest is in area of systems biology. Stochastic approaches, on the other hand, are mainly concerned with the quantitative and probabilistic aspects of biological systems, supporting computationally based simulation and verification approaches to the analysis of living organisms.

The papers contained in this issue were selected among those presented at the workshops, then extended and additionally reviewed according to the standard policy of the TCS journal.

The first two papers are devoted to membrane systems. The first one, *An Infinite Hierarchy of Languages Defined by dP Systems* by Gh. Paun and M.J. Perez-Jimenez, deals with distributed P automata (dP automata). It solves an open problem in the area of membrane systems by proving that dP automata induce a proper infinite hierarchy of the recognized languages according to the number of components (P automata) in the system. It is shown that the languages of particular variants of dP automata are languages of right-linear simple matrix grammars. The paper also discusses the relationship between the balanced and the non-balanced way of splitting the input string among the components. In the second paper, *Modeling Dependencies and Simultaneity in Membrane System Computations*, G.M. Pinna and A. Saba develop a Petri net view of membrane systems which is based on zero-safe Petri nets. They characterize dependences and simultaneity in the occurrences of rules in membrane system computations, relate membrane systems to Petri nets, and then introduce new notions of event structures with the aim of capturing precisely the concurrency phenomena appearing in the evolutions of membrane systems.

The second group of four papers deals with process calculi. The first paper, *Processes in Space* by L. Cardelli and P. Gardner, presents a geometric process algebra based on affine geometry able to express several kinds of dynamic behaviours in 3D space. The paper combines the interaction primitives of the pi-calculus with geometric transformations by introducing a single new geometric 'frame shift' construct which applies a 3-dimensional affine transformation to an evolving process. The paper proves a relativity theorem which states that algebraic equations are invariant under the rigid body transformations. In the paper, *Reachability Problems in BioAmbients*, G. Delzanno and G. Zavattaro investigate the limits of the decidability of both the target and the spatial reachability in bioambients, analysing the impact of the merge capability used for fusing the contents of two sibling ambients. The paper shows that after removing the merge operation both the target and the spatial reachability are decidable by a reduction to a Petri net problem. If the merge operation is restricted to be monotone, then it is shown that the target reachability is undecidable, while the spatial reachability is still decidable. The third paper of this group is *Simulation Techniques for the Calculus of Wrapped Compartments* by M. Coppo, F. Damiani, M. Drocco, E. Grassi, E. Sciacca, S. Spinella and A. Troina. The paper defines a hybrid simulation method, combining the stochastic approach with

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ordinary differential equations for systems described in the Calculus of Wrapped Compartments in which one can express the compartmentalization of a biological system whose evolution is defined by a set of rewrite rules. The paper introduces a hybrid simulation algorithm for this calculus. Finally, in *Foundational Aspects of Multiscale Modelling of Biological Systems with Process Algebras*, R. Barbuti, G. Caravagna, A. Maggiolo-Schettini, P. Milazzo and S. Tini present a variant of CCS for modelling multiscale systems in a general way. The paper defines a labelled transition system semantics by following the approach in which actions are not instantaneous, but rather described by two separate starting and ending transitions. The paper changes the usual interpretation of the summation operator by making it similar to a parallel composition and allowing a process to be involved in several actions at the same time. The paper presents both a reduction semantics and a structured operational semantics, and demonstrates their correspondence.

The next group of papers is centred around stochastic aspects in modelling and analysis. In the first paper, *Measurable Stochastics for Brane Calculus*, G. Bacci and M. Miculan introduce a stochastic extension of the Brane Calculus. The proposed compositional structural operational semantics of a process is a measure of the stochastic distribution of possible derivations. The paper also discusses process equivalence and provides a stochastic semantics to brane systems. The next paper, *Lumpability Abstractions of Rule-based Systems* by J. Feret, T. Henzinger, H. Koeppl and T. Petrov, is concerned with abstractions of probabilistic transition systems aimed at reducing the combinatorial complexity intrinsic in the analysis of behaviour of biological systems. The paper demonstrates that a state space quotienting which preserves the stochastic semantics yields a sufficient condition for weak lumpability and that it gives rise to a backward Markov bisimulation between the original and the aggregated transition system. In the third paper, *Typed Stochastic Semantics for the Calculus of Looping Sequences*, L. Bioglio, M. Dezani-Ciancaglini, P. Giannini and A. Troina consider a quantitative term rewriting formalism which can be used to model and analyse the evolution of microbiological systems. For such a formalism, the paper proposes an operational semantics that considers the types of the species in order to derive the stochastic evolution of the system. The final paper in this group, *Stochastic Simulation of Multiple Process Calculi for Biology*, by M.R. Lakin, L. Paulevé and A. Phillips, investigates issues involved in the simulation of many stochastic process calculi developed for biological modelling. To avoid resorting to custom simulation algorithms, the paper proposes instead a generic abstract machine that can be suitably adapted to work with several process calculi and simulation methods.

The last group of two papers is concerned with biological regulatory networks. In the first paper, *An Abstraction Theory for Qualitative Models of Biological Systems*, R. Banks and L.J. Steggles investigate multi-valued networks that are an important qualitative modelling approach used within the biological community. In particular, they address problems related to the state space explosion problem encountered in the verification of multi-valued networks. The paper presents an abstraction theory for multi-valued networks, illustrated by two detailed case studies based on existing biological models, which results in the reduction of the state space of a model without losing its key behavioural properties. The second paper, *Integrated Regulatory Networks (IRNs): Spatially Organized Biochemical Modules* by J.-L. Giavitto, H. Klaudel and F. Pommereau, is concerned with the modelling and analysis of the regulation processes in multi-cellular biological systems, such as tissues. The paper presents in a comprehensive way a newly developed modelling framework which supports information about cell's physical state and environment, its transition system based semantics, as well as a prototype implementation that allowed preliminary experiments on some applications related to biology.

All the papers were reviewed by at least three referees. We thank all the authors and reviewers for doing an excellent job; without their enthusiastic work and support, this volume would not have been possible.

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